Journal of the American Society of Cytopathology (2016) 5, 145–153

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jascyto.org/

ORIGINAL ARTICLE

Cytology as a screening tool for anal squamous intraepithelial lesion for HIV positive men: 10-year experience in an inner city hospital

Gina E. Johnson, MD[a,*], Minh Ly Nguyen, MD[b], Uma Krishnamurti, MD[a], Shabnam Seydafkan, MD[c], Lisa Flowers, MD[d], Shahrzad Ehdaivand, MD[a], Marina Mosunjac, MD[a]

[a] *Department of Pathology and Laboratory Medicine, Emory University, 1364 Clifton Rd. NE, Atlanta, Georgia*
[b] *Department of Obstetrics and Gynecology, Emory University, Atlanta, Georgia*
[c] *Post-Doctoral Research Fellow, Emory University, Atlanta, Georgia*
[d] *Division of Infectious Disease, Department of Internal Medicine, Emory University, Atlanta, Georgia*

Received 1 July 2015; received in revised form 26 August 2015; accepted 26 August 2015

KEYWORDS
Anal cytology;
Anal Pap;
Cytology histology correlation;
AIN;
Anal carcinoma HIV

Introduction Human papillomavirus (HPV) and anal carcinoma are prevalent in high-risk patients including human immunodeficiency virus (HIV)-positive patients. There are currently no clear guidelines for screening, however. We assessed anal cytology specimens and HPV testing at an inner-city hospital by correlating anal cytology with anal biopsy (bx), and evaluated if results differed with traditional proctoscopy (TP) or high-resolution anoscopy (HRA).

Materials and methods 209 anal cytology and subsequent biopsies taken during the period 2003-2014 from 152 male patients were reviewed. Demographic data for age, sex, HIV, HPV, cytology, histology, and the method of biopsy were analyzed.

Results All specimens were followed by a biopsy within a period of 6 months. Ninety-seven percent of patients were HIV-positive and 43% had AIDS. Lesions most diagnosed on cytology were low-grade squamous intraepithelial lesion (LSIL) (52%) and atypical squamous cells of undetermined significance (ASC-US) (21.5%). Lesions most diagnosed on bx were anal intraepithelial neoplasia (AIN) grade 2-3 (52%) and AIN grade 1 (37%). Almost all ASC-US cases tested for HPV were positive (97%). There was cytology histology correlation in 48% of LSIL and 83% of high-grade squamous intraepithelial lesions. Anal cytology had 97% sensitivity in detecting AIN and carcinoma and a positive predictive value of 96%. There was no difference in rate of detection of AIN 1and AIN 2-3 on bx using TP versus HRA.

Authors have no financial relationships to disclose.

*Corresponding author: Gina E. Johnson, MD; Department of Pathology and Laboratory Medicine, Emory University Hospital, 1364 Clifton Rd NE, Atlanta, GA 30322; Tel.: 404-712-8211 (work); Fax: 404-712-2052.
E-mail address: gejohn4@emory.edu (G.E. Johnson).

http://dx.doi.org/10.1016/j.jasc.2015.08.003

Conclusion Screening in high-risk patients detected almost all high- and low-grade squamous intraepithelial lesions, however, anal cytology alone could not predict the degree of dysplasia. It may be prudent to perform anal bx in all atypical anal cytology. Clear guidelines are needed for screening of a high risk population.

Introduction

Anal cancer is a rare but increasing disease. With 1.8 new cases per 100,000 men and women per year, 7270 new cases were predicted in 2015 alone. The lifetime risk of developing or dying from anal cancer is approximately 0.2%. Historically, women have had a higher incidence of anal cancer than men in the United States; nevertheless, the overall incidence of anal cancer has been increasing steadily over the past decade almost equalizing the incidence in both sexes.[1] Certain populations, such as human immunodeficiency virus (HIV)-positive patients, HIV-positive men who have sex with men (MSM), and immunocompromised patients, are at higher risk of anal cancer.[2,3] The biology of anal carcinoma is similar to cervical carcinoma in that it is caused by the human papillomavirus (HPV), particularly type 16. HPV affects 79 million people around the world and is now considered the most common sexually transmitted disease, affecting 38% of men attending a sexually transmitted disease clinic.[4] HPV infects the basal keratinocytes of squamous epithelium via micro-abrasions, or disruptions.[5]

There are increasing numbers of HIV-positive patients taking highly active antiretroviral therapy (HAART), but the number of cases of anal carcinoma has only increased during this time. Though HAART partially restores immune function, it does not lead to the regression of anal intraepithelial neoplasia (AIN).[2,6] Post-transplantation immunosuppression is known for increased HPV-associated anogenital lesions and a broad reported increase of anal carcinoma in women status-post renal transplantation, with risk ratios ranging from 10-fold to 100-fold.[7-11] A history of genital squamous lesions is often due to HPV infection, as many genital lesions are caused by the persistence of high-risk HPV infection.[12]

Currently, the Infectious Disease Society of America has weak recommendation guidelines for HPV screening in patients with HIV. Their guidelines recommend that MSM, women with a history of receptive anal intercourse or abnormal cervical Pap test results, and all HIV-infected persons with genital warts should have anal cytology testing.[13] Although these guidelines are available, a recent review highlights the paucity of screening-related research and encourages that more studies are needed to further define stronger screening standards.[14] With an increasing incidence of anal carcinoma, there is a need for education about diagnosing anal squamous lesions on anal cytology.[15] In this study, we aimed to assess the adequacy of using anal cytology as a predictor of anal squamous intraepithelial lesion (SIL) by comparing anal cytology and HPV status to histology results in a predominately HIV-positive population. We also aimed to determine if the methods of collecting anal biopsies influence the number of low-grade or high-grade SIL identified.

Materials and methods

After consent was obtained through Emory University's institutional review board, data analysis was performed over a 10-year period (2003-2013) at an inner city hospital. Anal cytology specimens, HPV results, and anal biopsy results from 152 men were evaluated. The patient population was predominately HIV-positive (97%). At the time of first anal cytology, a CD4-count was used to determine HIV versus AIDS status. The HIV status for the remainder of the population (3%) was unknown. During the years 2007 to 2011, HPV status was determined by the DIGENE Hybrid Capture II High-Risk HPV DNA test, which tested for HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68. From 2011 to the present, the GEN-PROBE APTIMA HPV assay has been used, which screened for the same 13 types of high risk HPV as the DIGENE test, with the addition of type 66. Neither of the two tests used were able to discriminate between the high-risk types.

Anal cytology samples were collected using a moistened Dacron swab inserted to the anal canal approximately 3 cm above the anal verge. The swab was then rotated 10-15 times in a cone-shaped arc and withdrawn. The swab was then transferred to a vial of Sure Path preservative processed according to the manufacturer's instructions and then stained using a modified Papanicolaou staining procedure.

The biopsy specimens were collected using 2 methods. In the first method, called traditional proctoscopy (TP), the patient was taken to the operating room, given general anesthesia and placed in a lithotomy position. A complete evaluation of the perianal area and anal canal using an anoscope was performed to assess for any gross lesions, ulcerations, or masses. No magnification was used for visual inspection with traditional proctoscopy. Five percent acetic acid was applied to the perianal area and the anal canal. A systematic 4-quadrant biopsy of the anal canal and anal verge was performed. In addition, any areas staining acetowhite or abnormal appearing were biopsied, including lesions in the perianal region.